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Observations on the direct influence of variations of arterial pressure

presented by the author

OBSERVATIONS ON THE DIRECT INFLUENCE OF VARIATIONS OF ARTERIAL PRESSURE UPON THE RATE OF BEAT OF THE MAMMALIAN HEART.

By H. NEWELL MARTIN, M. A., M. D., D. Sc. With Plate XV.

THE earliest observations on this subject, so far as I know, were made by Marey (Recherches sur le pouls au moyen d'un nouvel appareil enrégistreur. *Mémoires de la Société de Biologie*, 1859); but as the extrinsic cardiac nerves were not divided in his experiments, and a rise of blood pressure is now known to stimulate the medullary cardio-inhibitory and accelerator nerve centres, the results obtained by him give really no information as to the direct influence of increased aortic tension upon the rate of the heart's beat. Since then others have experimented, previously dividing the extrinsic cardiac nerves, Ludwig and Thiry in 1864 (*Sitzb. d. Akad. d. Wissensch. zu Wien*) leading the way, but the general result is that the matter has been left in a highly unsatisfactory state. Some find that variations of arterial pressure have no effect on a heart whose venous connections with other parts of the body have been severed; others that arterial pressure and pulse rate rise and fall together; others that the pulse quickens when arterial tension is lowered and *vice versa*. Finally, Tschirjew (*Arch. f. Anat. u. Physiologie, Jahrgang* 1877, p. 116), the latest writer on the subject, finds all of the above effects in different cases: as the result of an extensive series of experiments he comes to the conclusion that after section of all the extrinsic heart nerve paths, "any considerable and rapid elevation of blood pressure may directly stimulate either the inhibitory apparatus in the heart, or its motor ganglia, and the pulse rate accordingly be increased or diminished, or in more rare cases remain unaltered." Such contradictory results obtained by a number of competent workers lead naturally to the suspicion that some error is involved in the methods of experiment employed; the nature of this error is not, I think, far to seek. The methods used to vary arterial pressure have been such as cause variations also in several other conditions which

either are known to influence the heart, or may possibly do so; nevertheless all these secondary actions have been unheeded: their relative prominence in any given experiment has not been noted, and any change in the pulse rate has been ascribed solely to the changed arterial pressure. Under such circumstances it need cause no surprise that very inconsistent results should be obtained.

The higher aortic pressure is, the more force must be expended by the left ventricle in forcing open the semilunar valves; that is to say, the higher will be intraventricular systolic pressure. It is this influence only of increased aortic pressure which should be meant when its direct action upon the cardiac rhythm is spoken of; and to get pure results all other consequences of increased arterial tension which may influence the heart's rate of beat must be eliminated. This, however, has not been the case in any series of experiments with which I am acquainted.

Arterial pressure has commonly been increased by clamping the descending aortic, either in the thorax or abdomen. When this is done, however, we alter several other things in addition to arterial pressure—

(1.) The amount of blood returned to the right auricle in a given time is almost certainly altered, and therefore the rate of filling of the heart during diastole.

(2.) The pressure under which venous blood enters the right auricle is probably changed, and therefore intracardiac pressure at the end of the diastole.

(3.) The temperature of the blood returned to the heart by the systemic veins and, as a consequence, of the heart itself, is altered. The blood returned to the right auricle by the inferior cava is known to be warmer than that returned by the superior cava, which has not flowed through the hot abdominal organs. When the aorta is clamped the heart gets only the cooler superior cava blood, as the capillary tracts tributary to the inferior cava are no longer supplied with blood.

(4.) It is known that very slight chemical changes in the blood profoundly influence the heart's beat. To quote no other instance, Gaule has shown that the heart of a frog previously kept in the cold and exhibiting deficient functional power, may be restored to full vigor by circulating through it the extract of the heart of a frog kept previously at a higher temperature. Blood in its flow through the abdominal organs experiences important chemical

changes entirely differing from any undergone in other regions of the body. If, therefore, we circulate blood through head, neck and fore limbs only, and return it again and again to the heart without exposing it to the action of kidneys, spleen and liver, we very soon have a liquid to deal with which is essentially different from that which flowed through the heart before the aorta was ligated.

Of course when the arterial pressure is lowered by opening the previously clamped aorta all of the above possible disturbing actions occur in the opposite direction.

Another method which has been employed to raise arterial pressure is to inject blood from another animal into the carotid of the animal experimented upon. This also involves several possible sources of error. (1) Venous inflow during cardiac diastole is almost certainly changed. (2) Venous pressure and, therefore, intracardiac diastolic pressure are probably altered. (3) The injected blood may differ chemically from that already in the vessels, and directly act upon the heart. (4) Unless extreme care be taken the temperature of the injected blood will be less or greater than that of the already circulating blood, and will alter the temperature and, therefore, the rhythm of the heart. To the above objections it may be added that only slight increase of arterial pressure can be brought about in this way; as is proved by Worm Müller's experiments. (*Arbeiten aus d. physiol. Anstalt zu Leipzig*, 1873).

When blood pressure is lowered by bleeding, diastolic inflow and pressure are altered, as well as arterial pressure; and also probably the chemical metabolisms experienced by the blood in its flow through different organs.

As some one, at least, of the above secondary influences has been present in all previous experiments as to the influence of variations of arterial pressure upon the pulse rate, it is clear that none of these experiments, interesting and important as their results are in many cases, are really capable of affording an answer to the question in hand, viz: what is the influence, if any, pure and simple, of increased aortic pressure (*i. e.* of increased systolic pressure within the left ventricle) on the pulse rate. It is, therefore, not necessary to consider in detail the experiments of previous writers. All are vitiated more or less by secondary changes

which have occurred along with the variations of arterial pressure; and the number of these possible complications, and their varying degree in different experiments, affords a sufficient explanation of the contradictory results obtained.

As regards the frog's heart, there is more agreement between observers, and the experimental conditions have usually been more satisfactory. Usually the auricle is supplied steadily with liquid of constant composition and at constant pressure from a Marriott's flask; but even here, so far as I know, the arterial cannula has always been inserted into the ventricle and, therefore, beyond the semilunar valves. As a necessary consequence of this, not only systolic ventricular pressure (which normally is the thing changed by varied arterial pressure), but also diastolic intraventricular pressure has been varied. I accordingly suggested to two of my pupils that they should undertake a fresh examination of this question by better methods, on the hearts of frogs and chelonia. Some results of their work will be found on subsequent pages of the present number of this Journal.

The question involved is clearly one of great importance. In almost every experiment relating to cardiac physiology arterial pressure is altered: and it is essential to know exactly the direct influence of this factor on the heart, before further conclusions can be legitimately arrived at. I have, therefore, lately carried out a large number of experiments as to the direct influence of variations of arterial pressure upon the pulse, making use of the dog's heart completely isolated physiologically from every other organ, but the lungs: the method of isolation, which essentially consists in closing the whole systemic circulation except that through the coronary vessels of the heart itself, was described by me in the last number of this Journal (Vol. II, No. 1, p. 119); as the apparatus has since been modified only in some points of detail, I here reproduce, as Plate XV, the figure used in illustrating the previous paper, in order to assist in the description of my more recent experiments.

The right and left carotid arteries, *o* and *r*, have cannulas placed in them, the right subclavian, *w*, is ligatured, and a cannula is put in the left subclavian, *m*. Then the aorta is ligated immediately beyond the origin of the left subclavian: the vena cava inferior and the azygos vein are tied, and a cannula put in the superior cava. Fresh defibrinated strained and warmed blood is

now run in by the superior cava; at the same time the cannula on the right carotid is opened, and blood drawn from it until there is reason to believe that all the blood originally in the heart and lungs of the animal has been washed out; the carotid is then again clamped, and the superior cava a few seconds later, when the heart and lungs have been tolerably well filled with blood. The animal is then transferred to the warm moist chamber, *K*, the cannula of the superior cava is connected with one of the Marriott's flasks, 27 or 28, from which a nutrient liquid is sent into the heart under a uniform pressure, which in the experiments described below was that exerted by a column of blood 10 centimetres in height. The left carotid, *o*, is connected with the outflow tube, 21, and the cannula in the subclavian with a mercurial manometer, 26, the pen of which writes on the paper of a kymographion in the usual manner. As soon as one Marriott's flask is empty its connection with the heart is shut off, and that of the other (which has been meanwhile closed) is freed by opening the proper one of the clamps, 1 or 2, and closing the other. The nutrient liquids employed in the experiments below described were (1) fresh defibrinated strained dog's blood; (2) the same diluted with an equal bulk of 0.5 per cent. solution of sodium chloride in distilled water. I may here state that in other cases I have used with success (3) defibrinated dog's blood with one-third its bulk of 0.7 per cent. sodium chloride solution; and (4) defibrinated calf's blood.

Under these conditions almost all of the ordinary collateral results of increased or lowered arterial pressure can be eliminated. By closing more or less completely the stop-cock, 22, arterial pressure can be raised; by opening the stop-cock wider it can be diminished. Meanwhile rate of supply to the right auricle, the temperature of the liquid sent into it, and the composition of this liquid are unvaried; all these disturbing elements are thus got rid of. I have said above that "almost" all secondary effects can be eliminated; the *almost* is due to the varied coronary circulation; when aortic pressure is high this must be greater than when that pressure is low; so far I see no method of eliminating this possible source of error; but in recent years much evidence has been accumulated to shew that if the flow of blood through an organ is sufficient to nourish it (*i. e.*, does not fall below the starvation limit), and is under a lower pressure than such as ruptures the vessels or otherwise mechanically impedes

the action of the organ, there is much reason to believe that variations in blood supply have no immediate influence on its functional activity. The experiments detailed below give further support to this view: as will be seen, variations of arterial pressure ranging between 25 and 150 mm. of mercury have no influence whatever upon the heart's rhythm, although considerably more blood must flow through the coronary system under the higher than under the lower pressure.

In the experiments described below the heart was always left in the warm chamber at least half an hour before observations were made, and longer if the thermometer did not shew that the temperature was then uniform and had been for some five or ten minutes. The animals during the isolation of the heart were sometimes placed under the influence of morphia, sometimes of curari, and sometimes of chloroform; these various agents were used to eliminate chances of error due the possible toxic action of any one of them on a regulatory mechanism in the heart, though when fresh unpoisoned defibrinated blood is run for hours through the heart after its isolation, there can be little doubt that any poison absorbed by the organ during the preliminary observation is thoroughly washed out. The animals used were small dogs, weighing from 6 to 7.5 kilos. Uniform artificial respiration was kept up by means of a small water engine.

When temperature had become constant, the connection between a full Marriott's flask (containing about 700 c. c. of liquid) and the heart was opened. A minute or two was allowed to elapse, to get a steady inflow current; then arterial pressure was raised by partially closing the stop-cock, 22, or lowered by opening it wider. Tracings were taken for from two to six minutes with arterial pressures varied in this way; then the observation ceased. Meanwhile the other Marriott's flask was filled; and after some minutes another observation was made while it was connected with the heart; and so on, so often as seemed desirable. In all cases the experiment came to an end long before the heart shewed signs of abnormal or irregular action; indeed in most instances it was subsequently used for preliminary observations on the influence of other conditions, as varied venous pressure or varied temperature on the pulse rate.

The results arrived at may be summed up as follows:

1. *When the pressure under which blood of uniform temperature and composition is steadily supplied to the right auricle does not*

exceed that due to a column of blood ten centimetres in height, no variation of arterial pressure which can be brought about by opening or closing more or less completely the outflow stop-cock, has any influence whatever on the rhythm of a heart isolated from all other organs of the body except the lungs, provided arterial pressure be not kept at a very low level for a considerable time. In other words, within very wide limits, changes in arterial pressure have no influence whatever upon the pulse rate.

2. *If the outflow stop-cock be widely opened and arterial pressure lowered to less than twenty millimetres of mercury, this has no direct influence on the pulse rate; but it has probably an indirect influence. For a minute or more the heart beats recur at the same intervals, but after that time, if the low pressure be still maintained, the pulse sometimes becomes slower, probably from deficient nutrition of the heart dependent on insufficient flow through the coronary vessels.*

3. *If the pressure at which venous blood enters the right auricle be considerable (due to a column of blood forty centimetres in height), and if simultaneously the arterial exit be greatly narrowed by closing the outflow stop-cock, then arterial pressure at first rises greatly without any alteration in the pulse rate; but ultimately attains a very high level at which the cardiac rhythm becomes extremely irregular. Beats occur which somewhat resemble those produced by feeble pneumogastric stimulation. If the arterial resistance be now diminished, markedly dicrotic beats occur for some twenty or thirty seconds, until arterial pressure again falls to a normal level, when the original pulse rate is resumed. The conditions when the irregular beats are observed are clearly pathological: a filling of the heart under a pressure in the venæ cavæ equal to forty centimetres of blood (twenty-nine millimetres of mercury) probably never occurs normally combined with great arterial resistance.*

In the present article I shall confine myself to what may be called normal variations of arterial pressure, that is to say, for small dogs, variations between 25 and 160 millimetres of mercury. The result under the above heading 2 is undoubtedly abnormal, and due to commencing death of the heart; and the results indicated under number 3 are probably due either to the reception by the left ventricle in each diastole of more blood than, under the resistance opposed to it, it can pump out in one systole, or to a direct stimulation of inhibitory mechanisms in the heart by the pathological pressure within the ventricle. This irregular beat

with very great arterial resistance has been noted by Haidenhain, and I may here state that Knoll's opinion that it really means not a slowed heart beat, but a quick irregular beat which the manometer does not properly record, is incorrect; direct observation of the exposed heart is conclusive as to the fact that the beats are not quick and irregular, but really slow, and frequently dicrotic.

On the results numbered 2 and 3 above I desire to make further observations before publishing detailed conclusions. Hitherto so soon as I have observed indications of them I have at once raised or lowered arterial pressure so as to prevent death or injury to the heart. As regards point 1, the three tables below speak for themselves. They are selected from a dozen experiments which are perfectly concordant, and they have been so selected that a different drug was given to the dog during the preliminary operation of isolating the heart in each case. The venous inflow was always so proportioned to the resistance to arterial outflow that pressure in the subclavian during the intervals between any two observations was kept at a point from which arterial pressure could be considerably raised without the variation passing beyond a physiological limit; but at the same time, a pressure sufficient to keep the heart in a functional condition for a long time.

Venous pressure in all the experiments recorded below was that due to a column of nutrient liquid (defibrinated dog's blood, or the same diluted with an equal volume of sodium chloride solution) ten centimetres in height, or very near that; it is not well practicable to measure exactly in every experiment the difference in level between the cannula in the superior cava and the lower end of the tube for the entry of air into the Marriott's flask; but errors of a few millimetres in this regard are of no importance: so long as the pressure is constant during an observation a knowledge of its absolute amount within 5 or 6 millimetres of blood is of no consequence.

The tables are constructed as follows: Temperature in the moist warm chamber having become constant, the kymographion was started and tracings taken for from two to seven minutes. During this time the stop-cock, 22, was opened wider, or more closed, or opened and then closed, or *vice versa*, and consequently arterial pressure was altered. A number of such observations having been made the tables were constructed from the tracings obtained: suppose the time to be 2 h., 20′, 10″, then arterial pressure is

measured at that time and at 2 h., 20′, 20″. Half the sum of these is taken as the mean pressure during the intervening ten seconds. The pulse rate is counted for this ten seconds, multiplied by 6, and the product given as the rate of heart beat per minute, with the mean arterial pressure obtained as above. So far as absolute results are concerned, it is seen that the mean arterial pressure arrived at in this way is open to some error, and had changes in it been accompanied by changes in the pulse rate, more accurate methods of arriving at the true mean arterial pressure during each ten seconds would have to be employed. But as very great variations of mean arterial pressure were used and as the experiments shew that none of them, within the limits described above as physiological, cause any change in the rate of the heart's beat, it is clearly unnecessary to resort to planimetry or other troublesome methods so as to avoid possible errors of a few millimetres in the measurements. When gross variations of arterial pressure from 30 to 150 mm. of mercury cause no change, it is not worth while to spend time in endeavoring to exclude possible errors of ten or even fifteen millimetres of mercury pressure; and the possible limits of error in my measurements never reached the less of those quantities. When the lungs are kept well extended and the artificial respiration apparatus works with tolerably slow powerful blasts, marked respiratory waves are seen on the tracings of arterial pressure, unless this fall to 50 millimetres of mercury or thereabouts, when they disappear. As these rhythmic rises and falls of arterial pressure render it more difficult to correctly arrive at the mean pressure, I have usually eliminated them by arranging my water engine so as to work with rapid short strokes; then respiratory variations of arterial pressure entirely disappear from the manometer tracings.

In the experiments recorded below the heart had been physiologically isolated from all other organs but the lungs for some considerable time before the recorded observations were made; the muscles of the body in general were often already in marked rigor before the first observation was made and always long before the last. When the words "no record" appear in the details of an observation, some one or more of the pens was not writing, so that either time, pressure, or pulse rate, could not be determined. The temperature given is that of the warm chest in which the animal lay.

Experiment A.

October 13, 1881. Small dog, narcotised with morphia during the operation of isolating the heart. Nutrient liquid 1,400 cub. cent. of defibrinated dog's blood drawn from two other animals. Arterial pressure measured in left subclavian. Heart isolated and animal put in warm chamber at 4 h. 10′, P. M.

Observation.	Time.	Temperature in degrees C.	Arterial Pressure in mm. of mercury.	Pulse Rate per minute.
I.	4 h. 44′ 00″	37°	137	147
	" 10		134	147
	" 20		131	146
	" 30		132	147
	" 40		116	147
	" 50		89	147
	4 h. 45′ 00″		74	147
	" 10		83	150
	" 20		109	147
	" 30		124	147
	" 40		134	150
	4 h. 46′ 00″		149	150
	" 10		142	149
	" 20		120	147
	" 30		98	147
	" 40		83	150
	" 50		99	147
II.	4 h. 58′ 50″	37°	133	147
	4 h. 59′ 00″		134	149
	" 10		139	147
	" 20		143	150
	" 30		144	150
	" 40		142	149
	" 50		138	149
	5 h. 00′ 00″		136	148
	" 10		129	150
	" 20		104	150
	" 30		82	150
	" 40		87	150
	" 50		117	151
	5 h. 01′ 00″		123	148
	" 10		129	151
	" 20		133	150
	" 30		130	150
	" 40		110	150
	" 50		90	151

EXPERIMENT A.—*Continued.*

Observation.	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
III.	5 h. 17′ 00″	37°	112	150
	" 10		119	150
	" 20		102	150
	" 30		80	150
	" 40		87	No record.
	" 50		100	150 (?)
	5 h. 18′ 00″		108	No record.
	" 10		114	150
	" 20		119	150
	" 30		125	No record.
	" 40		126	151
	" 50		112	150
	5 h. 19′ 00″		89	150
IV.	5 h. 29′ 40″	37°	80	150
	" 50		81	153
	5 h. 30′ 00″		80	156
	" 10		82	150
	" 20		93	156
	" 30		104	153
	" 40		110	153
	" 50		112	156
	5 h. 31′ 00″		111	153
	" 10		112	150
	" 20		99	150
	" 30		80	156
	" 40		82	156
	" 50		93	153
	5 h. 32′ 00″		102	156
	" 10		100	156
	" 20		86	156
	" 30		85	150
	" 40		97	156
	" 50		102	152

In observation I, arterial pressure varied between 74 and 149 millimetres of mercury (101 per cent.) and the pulse rate between 147 and 150 per minute (2 per cent.). In observation II, arterial pressure varied between 82 and 144 millimetres of mercury (75.6 per cent.) and the pulse rate between 147 and 151 per minute (2 per cent.). In observation III, arterial pressure varied between 80 and 126 millimetres of mercury (57.5 per cent.) and

the pulse rate between 150 and 151 per minute (0.66 per cent.). In observation IV, arterial pressure varied between 80 and 112 millimetres of mercury (40 per cent.) and the pulse rate between 150 and 156 per minute (4 per cent.).

Experiment B.

October 15, 1881. Small dog, curarised during the preliminary operation. Nutrient liquid 1,350 cub. cent. of defibrinated dog's blood taken from two other animals. Arterial pressure measured in left subclavian. Operation completed and animal placed in warm chest at 1 h. 50′, P. M.

Observation.	Time.	Temperature in degrees C.	Arterial Pressure in mm. of mercury.	Pulse Rate per minute.
I.	2 h. 17′ 50″	34.5°	53.5	120
	2 h. 18′ 00″		78.5	120
	" 10		116.5	120
	" 20		No record.	No record.
	" 30		No record.	No record.
	" 40		86	120
	" 50		75	120
	2 h. 19′ 00″		69	120
	" 10		66	120
	" 20		80.5	122
	" 30		102.5	122
	" 40		114	121
	" 50		121	120
II.	2 h. 44′ 00″	35°	53	117
	" 10		57.5	117
	" 20		84	117
	" 30		117	123
	" 40		136	114
	" 50		145	118.5
	2 h. 45′ 00″		104	114
	" 10		67	118.5
	" 20		51	114
	" 30		49	117
	" 40		49	117
	" 50		35	117
	2 h. 46′ 00″		27	114
	" 10		25	117
	" 20		23	117
	" 30		22	114

EXPERIMENT B. OBSERVATION II.—*Continued.*

Observation.	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
II.	2 h. 46′ 40″	35°	22.5	114
	" 50		22.5	113
	2 h. 47′ 00″		21	111
	" 10		20	111
	" 20		25	114.5
	" 30		45	110
III.	2 h. 54′ 50″	35°	148	108
	2 h. 55′ 00″		116	108
	" 10		78	112
	" 20		56	108
	" 30		43	109.5
	" 40		38	108
	" 50		41	108
	2 h. 56′ 00″		51	108
	" 10		57	108
	" 20		89	112
	" 30		131	111
	" 40		143	110
IV.	3 h. 27′ 40″	35°	72.5	99
	" 50		87.5	102
	3 h. 28′ 00″		99.5	100
	" 10		117.5	99
	" 20		128	102
	" 30		140	103
	" 40		No record.	No record.
	" 50		No record.	No record.
	3 h. 29′ 00″		No record.	No record.
	" 10		91	102
	" 20		73	102
	" 30		59	102
	" 40		43	102
	" 50		44	102
V.	3 h. 31′ 20″	35°	63	98
	" 30		81	102
	" 40		98	98
	" 50		110	99
	3 h. 32′ 00″		119	100
	" 10		No record.	No record.
	" 20		No record.	No record.
	" 30		No record.	No record.
	" 40		No record.	No record.

EXPERIMENT B. OBSERVATION V.—*Continued.*

Observation	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
V.	3 h. 32′ 50″	35°	127	101
	3 h. 33′ 00″		106	102
	" 10		70	102
	" 20		54	101
	" 30		47	99
	" 40		55	100.5
	" 50		72	103
	3 h. 34′ 00″		89	102
	" 10		104.5	102
	" 20		112.5	101.5
	" 30		122	103
	" 40		130	102
	" 50		131	103
	3 h. 35′ 00″		111	104
	" 10		80	102
	" 20		65	100
	" 30		40	102
	" 40		51	102
	" 50		56	102
VI.	3 h. 40′ 55″	35°	50.5	102
	3 h. 41′ 05″		58.5	101
	" 15		64	102
	" 25		64	102
	" 35		66	102
	" 45		80	102
	" 55		100	102
	3 h. 42′ 05″		114	102
	" 15		101	102
	" 25		71	102
	" 35		61	102
	" 45		75.5	103
	" 55		98.5	102
	3 h. 43′ 05″		112	104
	" 15		102	103
	" 25		74	102
	" 35		56	101
	" 45		45	100
	" 55		33	102
	3 h. 44′ 05″		25	102
	" 15		23	102
	" 25		22	104
	" 35		18.5	102
	" 45		17.5	103

In observation I of the above experiment arterial pressure varied between 53.5 and 116.5 millimetres of mercury (117 per cent.) and the pulse between 120 and 122 per minute (1.6 per cent.). In observation II, arterial pressure varies between 20 and 145 millimetres of mercury (625 per cent.) and the pulse rate between 110 and 118.5 per minute (nearly 8 per cent.); this it will be seen on closer examination is one of the cases above referred to, which lead to the suspicion that a continued arterial pressure (as measured in the subclavian) of less than 30 millimetres of mercury is insufficient to nourish the heart and leads to a slowing of its beat. Arterial pressure was kept below this limit for nearly one and a half minutes, and the pulse rate fell from 117 to 110. In observation III, arterial pressure varies between 38 and 148 millimetres of mercury (290 per cent.) and the pulse rate between 108 and 112 per minute (3.6 per cent.). In observation IV, arterial pressure varies between 43 and 140 millimetres of mercury (225.5 per cent.) and the pulse rate between 99 and 103 per minute (4 per cent.). In observation V, arterial pressure varies between 40 and 111 millimetres of mercury (177.5 per cent.) and the pulse rate between 100 and 104 per minute (4 per cent.). In observation VI, arterial pressure varies between 17.5 and 114 millimetres of mercury (551.5 per cent.) and the pulse rate per minute between 100 and 104 (4 per cent.).

Experiment C.

October 26, 1881. Small dog, anæsthetised by chloroform during the operation of isolating the heart. Nutrient liquid 800 c. c. of defibrinated dog's blood mixed with 800 c. c. of 0.5 per cent. solution of pure sodium chloride in distilled water. Heart isolated and animal placed in warm chest at 12 h. 50′, P. M. When the series of observations detailed below was concluded the heart was still in good condition and was used for two hours for other experiments.

Observation.	Time.	Temperature in degrees C.	Arterial Pressure in mm. of mercury.	Pulse Rate per minute.
I.	1 h. 23′ 10″	37°	29	102
	" 20		30	103
	" 30		30	102
	" 40		30	102

EXPERIMENT C. OBSERVATION I.—*Continued.*

Observation.	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
I.	1 h. 23′ 50″	37°	33	103
	1 h. 24′ 00″		40	102
	" 10		46	103
	" 20		51	102
	" 30		59	102
	" 40		63	103
	" 50		56	101
	1 h. 25′ 00″		46	102
	" 10		40	102
	" 20		35	103.5
	" 30		42	102
	" 40		58	103
	" 50		70	102
	1 h. 26′ 00″		79	105
	" 10		80	104.5
	" 20		No record.	No record.
	" 30		40	105
	" 40		36	105
	" 50		26	105
II.	1 h. 33′ 20″	37°	40	100
	" 30		42	101
	" 40		43	102
	" 50		44	102
	1 h. 34′ 00″		37	102
	" 10		30	102
	" 20		25	102
	" 30		25	101
	" 40		28	101
	" 50		29	101
	1 h. 35′ 00″		28	102
	" 10		27	102
	" 20		29	101
	" 30		39	100.5
	" 40		52	102
	" 50		63	102
	1 h. 36′ 00″		72	102
	" 10		56	102
	" 20		32	102
	" 30		29	101.75
	" 40		41	101
	" 50		58	102
	1 h. 37′ 00″		68	102
	" 10		78	103
	" 20		87	103

EXPERIMENT C. OBSERVATION II.—*Continued.*

Observation.	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
II.	1 h. 37′ 30″	37°	93	105
	" 40		98	102
	" 50		101	102
	1 h. 38′ 00″		103	102
	" 10		88	102
	" 20		53	102
	" 30		29	102
	" 40		25	101
	" 50		25	100.5
	1 h. 39′ 00″		24	100.5
	" 10		24	102
	" 20		26	102
	" 30		27	102
	" 40		26	100.5
	" 50		28	100.5
III.	1 h. 57′ 30″	37°	28	96
	" 40		38	94
	" 50		24.5	97
	1 h. 58′ 00″		29.5	95
	" 10		33	96
	" 20		25	96
	" 30		14.5	99
	" 40		12	95
	" 50		14.5	96
	1 h. 59′ 00″		20	96
	" 10		24.5	96
	" 20		29	96
	" 30		34	98
	" 40		37.5	99
	" 50		30	96
IV.	2 h. 02′ 10″	37°	51	100
	" 20		54	100.5
	" 30		64	100.5
	" 40		76	102
	" 50		87	102
	2 h. 03′ 00″		94	102
	" 10		89	103
	" 20		56	105
	" 30		30	102
	" 40		37	102
	" 50		54	105
	2 h. 04′ 00″		70	108
	" 10		81	104

EXPERIMENT C. OBSERVATION IV.—*Continued.*

Observation.	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
IV.	2 h. 04′ 20″	37°	89	104
	" 30		95	106
	" 40		99	105
	" 50		106	105
	2 h. 05′ 00″		81	105
	" 10		39	105
	" 20		21	105
	" 30		24	104
	" 40		35	105
	" 50		50	108
	2 h. 06′ 00″		64	105
	" 10		77	108
	" 20		88	109
	" 30		81	110
	" 40		48	108
	" 50		23	108
	2 h. 07′ 00″		27	108
	" 10		42	107
	" 20		59	109
	" 30		73	110
	" 40		83	111
	" 50		77	109
	2 h. 08′ 00″		No record.	No record.
	" 10		19	109
	" 20		18	109
	" 30		19	109
V.	2 h. 17′ 20″	37°	25	105
	" 30		26	108
	" 40		29	105
	" 50		33	105
	2 h. 18′ 00″		40	106
	" 10		49	106
	" 20		53	106
	" 30		57	106.5
	" 40		63	106.5
	" 50		68	106.5
	2 h. 19′ 00″		71	106.5
	" 10		72	106
	" 20		73	106.5
	" 30		76	108
	" 40		77	106
	" 50		78	107
	2 h. 20′ 00″		77	105
	" 10		53	105

EXPERIMENT C. OBSERVATION V.—*Continued.*

Observation.	Time.	Temperature C.	Arterial Pressure.	Pulse Rate.
V.	2 h. 20′ 20″	37°	29	105
	" 30		23	105
	" 40		22	105
	" 50		24	105
	2 h. 21′ 00″		30	105
	" 10		39	105
	" 20		45	106.5
	" 30		53	105
	" 40		61	106.5
	" 50		66	106.5
	2 h. 22′ 00″		71	106.5
	" 10		No record.	No record.
	" 20		No record.	No record.
	" 30		76	106.5
	" 40		69	106.5
	" 50		46	106.5
	2 h. 23′ 00″		26	106.5
	" 10		22	106.5
	" 20		21	106.5
	" 30		20	106.5

In observation I of the above experiment, arterial pressure varied between 26 and 80 millimetres of mercury (207 per cent.) and the pulse between 101 and 105 per minute (4 per cent.). In observation II arterial pressure varied between 24 and 103 millimetres of mercury (329 per cent.) and the pulse rate between 100 and 105 per minute (5 per cent.). In observation III, arterial pressure varied from 12 to 38 millimetres of mercury (216.5 per cent.) and the pulse rate from 94 to 99 per minute (5 per cent.). In observation IV, arterial pressure varied between 18 and 106 millimetres of mercury (863 per cent.) and the pulse rate between 100 and 111 per minute (11 per cent.). In observation V, arterial pressure varied between 20 and 78 millimetres of mercury (290 per cent.) and the pulse rate between 105 and 108 per minute (less than 3 per cent.).

A critical examination of the preceding tables will, I think, shew conclusively that variations in arterial pressure within the limits indicated in them have no influence on the pulse rate of the

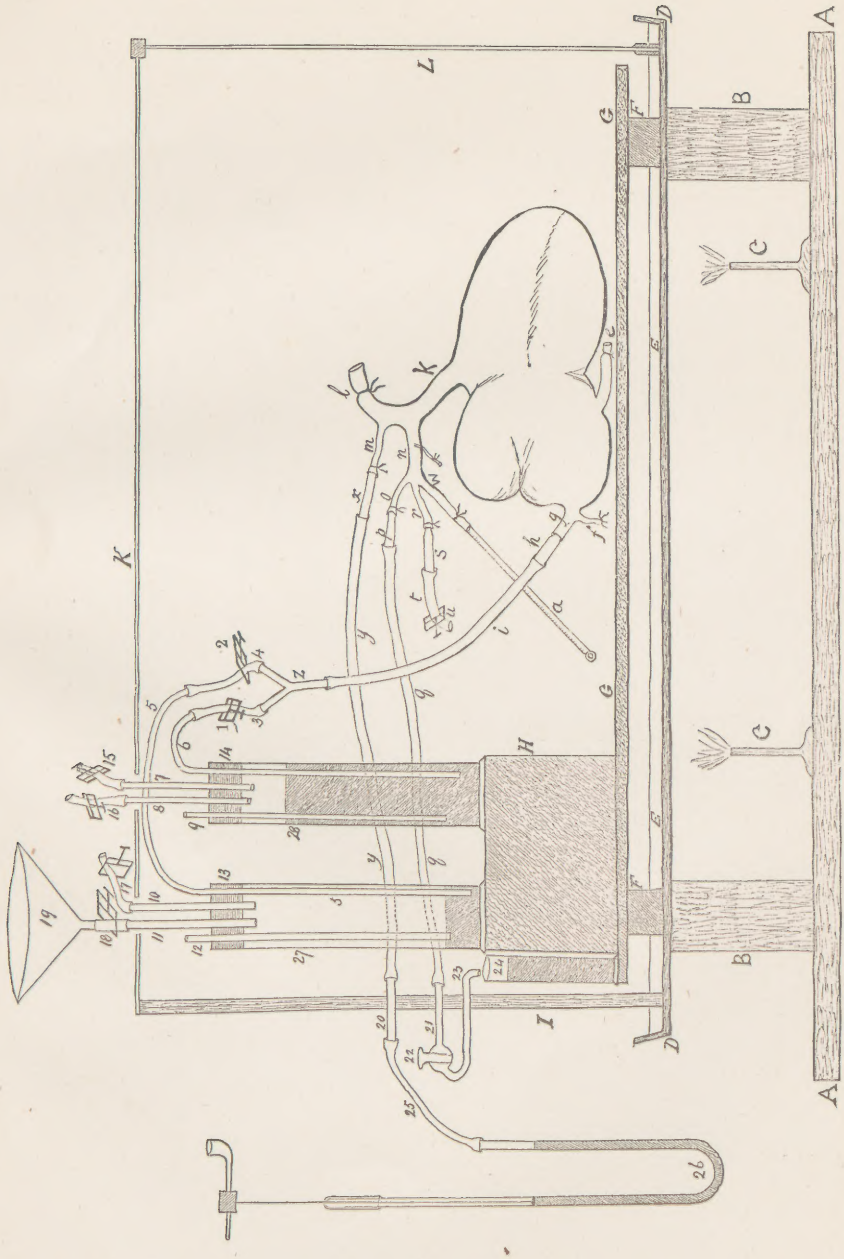
isolated dog's heart. In the great majority of cases the variations in the pulse rate fall clearly within the limits of error of the experiment (2–3 per cent.), while arterial pressure is greatly varied. Eliminating the obviously exceptional observations II, Expt. B, and IV, Expt. C, the average variation of arterial pressure in an observation was 204 per cent., and the average variation in the pulse rate 3.3 per cent.

That the possible sources of error will readily account for the pulse changes in most cases is clear — when it is remembered (1) that a mistake of one-sixth of a beat in counting out the pulse in any period of ten seconds appears in the tables as an error of one beat per minute; (2) that the temperature of the air pumped through the lungs and influencing the temperature of the blood was often unavoidably altered during the course of an observation as the doors of my present experiment room, which unfortunately is somewhat of a thoroughfare, were opened by passers-by from time to time. The latter influence is of great importance, as experiments which I hope shortly to publish, have proved that the dog's heart is, so far as its rhythm is concerned, extremely sensitive to slight variations in temperature.

Whatever the cause of the slight pulse-rate changes observed may be, it is at least clear that they are not dependent on varied aortic pressure, for there is no possible relationship, direct or inverse, to be detected between the two, when the whole series of observations is examined. In most cases great variations of arterial pressure are seen to occur without any change in the pulse rate, and then, a little later in the same observation perhaps, the pulse alters two or three beats a minute without any considerable simultaneous change in arterial pressure.

If the relationship between pulse rate and arterial pressure were invariable, even 3.3 per cent. of variation in the pulse per minute might clearly be significant: but as there is no such constant relationship, and the known sources of error fully account for such pulse-rate variations as were observed, they obviously mean nothing in this connection: and we may safely conclude that *within the limits of aortic pressure indicated by pressures varying between 25 and 140 millimetres of mercury in the subclavian, no change of pressure has any direct action upon the rate of beat of the isolated heart of the dog.*

Before concluding it is my duty and pleasure to acknowledge the willing and skilful assistance in the execution of my experiments rendered to me by Mr. H. H. Donaldson and Mr. Mactier Warfield, who not only undertook the tedious task of getting ready the apparatus for each experiment, but gave me most important help in carrying it through.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